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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/751,072	01/02/2004	Sven Eyckerman	2676-6264US	2266

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EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/751,072	EYCKERMAN ET AL.	
	Examiner	Art Unit	
	Zachary C Howard	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *9,10,12,14, 17-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8, 11, 13, 15, 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/24/04; 8/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-21 are pending in the instant application.

Election/Restrictions

Applicant's election of Group I, claims 1-8, 11, 13, 15, and 16 in the reply filed on 10/22/2004 is acknowledged. Applicant did not indicate whether this election was with or without traverse, but because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 9, 10, 12, 14, and 17-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Applicant's species election of the modification state of phosphorylation in the reply filed on 10/22/2004 is acknowledged.

Applicant's species election of a specific recombinant receptor including an EpoR ligand binding domain and an EpoR domain that comprises a heterologous bait polypeptide.

The examiner acknowledges the Applicant's notation that all elected claims are generic to the elected species.

Claims 1-8, 11, 13, 15, and 16 are under consideration.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8, 11, 13 and 15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 7, 12, 14, and 16 of copending Application No. 10/303157 in view of U.S. Patent No. 5,885,779 and further in view of Nicholson et al, published June 6, 2000 (PNAS 97(12): 6493-6498).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, claim 1 of 10/303157 recites a receptor comprising an extracellular ligand binding domain and a cytoplasmic binding domain comprising a heterologous bait polypeptide, wherein said recombinant receptor is activated by binding of a ligand to said extracellular ligand binding domain and by binding of a prey polypeptide to said heterologous bait polypeptide. The receptor of claim 1 of the instant application differs in that the receptor is inhibited by binding of a prey polypeptide to the bait domain. Other relevant claims of 10/303157 teach as follows: Claims 2-3 teach use of homomultimerizing or heteromultimerizing receptors in the recombinant receptor; Claims 4-5 and 7 of 10/303157 teach use of a bait that requires modification, such as phosphorylation, for binding of the prey molecule, and that the modification state is dependent on ligand binding; and claims 12, 14, and 16 teach use of a vector encoding the recombinant and eukaryotic cells comprising the vector.

The specification of 10/303157 does not teach a receptor wherein the receptor is inhibited by binding of a prey polypeptide to the bait polypeptide.

U.S. Patent No. 5,885,779 teaches a yeast two-hybrid system wherein the interaction of the bait and prey molecules causes inhibition of a transcriptional activator to which the bait is fused. This system can be used to screen for molecules that disrupt the bait-prey binding and lead to transcriptional activation. 5,885,770 further teaches (column 3, starting at line 60) advantages of using a system that relies on activation of a reporter to indicate disruption of bait-prey interaction. Such a system avoids pitfalls of a system relying on loss of a signal to indicate bait-prey disruption, wherein "failure to obtain expression may be caused by factors other than interference with the protein-protein interaction of interest. For example, compounds that interfere with transcription may score a false positive result. Similarly, compounds that generally inhibit cell growth may score a false positive result by appearing to interfere with the expression of a reporter gene that would confer survival on a restrictive medium."

Nicholson teaches a protein, SOCS-3, which inhibits signaling of the cytoplasmic gp130 domain of a chimeric receptor by binding to the gp130 domain.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the cytoplasmic domain of a receptor such as gp130, which is inhibited by prey (SOCS-3) binding, for cytoplasmic domain of the receptor taught by 10/303157, which is activated by prey binding. The person of ordinary skill in the art would be motivated to do so because 5,885,779 teaches that screening for compounds that disrupt protein-protein interactions is best achieved with a system that reduces false positives, and Nicholson teaches a receptor based system where disruption of the protein-protein interaction leads to activation. One would expect success because 10/303157 teaches a receptor where prey binding activates the receptor, and teaches its use for screening prey-bait binding interactions, and in the absence of other evidence, one would expect a screen using an inhibitor would work just as well because such systems have been developed for transcriptional based two-hybrid systems.

It would further have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the recombinant receptor as taught in claims 2-5 and 7 of 10/303157, to produce a receptor as taught by these claims but wherein the

receptor is inhibited by binding of a prey molecule. The person of ordinary skill in the art would be motivated to include an inhibitor for the same reasons as discussed above and because the further teachings of claims 2-5 and 7 are modifications of the receptor that allow for versatility in the type of receptors or bait used, and one would have expected success because, in the absence of other evidence, a receptor that is inhibited by prey binding would work just as well with these modifications as a receptor that is activated by prey binding.

It would further have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the vectors or eukaryotic host cell as taught in claims 12, 14, and 16 of 10/303157, to produce a vector that encodes a receptor that is inhibited by prey binding, or a host cell comprising said vector. One would have been motivated to do so because of the motivation to produce a receptor that is inhibited by prey binding as described above, and because a vector and host cell is necessary to produce such a receptor, and one would have expected success because, in the absence of other evidence, such a vector or host cell would be expected to work just as well to produce a receptor inhibited by prey binding as a vector or host cell that produces a receptor that is activated by prey binding.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 11, 13, 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it is unclear if the "domain that comprises a heterologous bait polypeptide" is meant to be a domain that comprises two heterologous proteins, or if the domain comprises a single bait polypeptide that is heterologous with respect to the ligand-binding domain. It is noted that page 15 of the

specification defines "heterologous bait polypeptide" as "within the receptor or fused to the receptor, but not in the ligand-binding domain of the receptor, there is a polypeptide that is not present in the non-recombinant receptor of which the cytoplasmic domain of the chimeric receptor is derived." For purposes of art rejections, claim 1 is being interpreted to mean either of these two definitions.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: 1) an extracellular ligand-binding domain; 2) a cytoplasmic domain comprising the cytoplasmic domain of a receptor and further comprising a heterologous bait polypeptide; 3) inhibition of the cytoplasmic domain of the receptor occurs when the bait polypeptide is bound by a fusion protein comprising a prey molecule and a heterologous inhibitor of the cytoplasmic domain of the receptor.

Claim 16 is rejected under 35 U.S.C. 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 16 is considered indefinite because a kit, by definition, must contain 2 or more elements and the interrelationships between the elements must be explicitly stated (see In re Venezia 530 F.2d 956 CCPA 1975).

Claim 16 is further indefinite because it is not clear what is meant by "a cloning vector allowing construction of the vector of claim 11." Because any cloning vector could be used to construct another vector, for the purposes of prosecution this claim is being interpreted to encompass any cloning vector.

The remaining claims are rejected for depending from an indefinite claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 11, 13, 15, and 16 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Nicholson et al, published June 6, 2000 (PNAS 97(12):6493-6498).

Nicholson teaches a chimeric receptor comprising the extracellular domain of the erythropoietin receptor (EpoR) and the transmembrane and cytosolic domains of the gp130 receptor. Nicholson teaches that binding of the SOCS-3 protein to the gp130 inhibits activation of the chimeric receptor. The chimeric receptor taught by Nicholson clearly anticipates all of the limitations of claim 1 of the instant application, including a recombinant receptor containing a ligand-binding domain (EpoR), a domain that comprises a heterologous bait polypeptide (gp130), and wherein the activation of said recombinant receptor is inhibited by binding of a prey polypeptide (SOCS-3) to the ligand-binding domain (gp130).

The recombinant receptor taught by Nicholson anticipates the further limitations of claims 2-8 of the instant application. The receptor taught by Nicholson is inactivated by binding of SOCS-3 to the receptor. Therefore, addition of a compound that disrupts bait-prey (receptor-SOCS3 binding) interaction would inherently activate the receptor. Chimeric receptors with EpoR extracellular ligand-binding domains form homomultimers upon binding the ligand EPO (Muthukumaran et al, 1997. Journal of Biological Chemistry. 272(8): 4993-4999. Cited here as an evidentiary reference only.) Nicholson further teaches (page 6497) that the cytoplasmic region of gp130 binds the protein SHP-2. The recombinant receptor EpoR-gp130 bound to SHP-2 meets the definition of a receptor that is heteromultimerizing. Binding of SOCS-3 to gp130 requires phosphorylation of the tyrosine residue 757 in gp130. Nicholson teaches (page 6497) that this residue on gp130 is phosphorylated in response to ligand-binding.

The teachings of Nicholson anticipate the further limitations of claims 11, 13, and 15. Nicholson further teaches (page 6494, Material and Methods) construction of a construct for expressing the recombinant receptor. Nicholson further teaches (Figure 4) transfecting 293T cells (human cells) with cDNAs expressing the receptor constructs.

Claim 16 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by "Expressions: A newsletter for gene cloning and expression", Invitrogen, 1999. Pg 1-16.

The Invitrogen brochure (page 2) describes kits containing vectors for one-step cloning into high level mammalian expression vectors. Any of these cloning vectors could be used to insert a vector encoding a recombinant receptor of claim 1. Therefore, the Invitrogen vectors meet all of the limitations of claim 16.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 11, 13, 15 and 16 are rejected under 103(a) as being unpatentable over Eyckerman et al, WO 01/90188, published November 29, 2001 and meriting priority to May 22, 2000, in view of U.S. Patent No. 5,885,779 and further in view of Nicholson et al, published June 6, 2000 (PNAS 97(12): 6493-6498).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the

application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claim 1 of WO 01/90188 recites a receptor comprising an extracellular ligand binding domain and a cytoplasmic binding domain comprising a heterologous bait polypeptide, wherein said recombinant receptor is activated by binding of a ligand to said extracellular ligand binding domain and by binding of a prey polypeptide to said heterologous bait polypeptide. The receptor of claim 1 of the instant application differs in that the receptor is inhibited by binding of a prey polypeptide to the bait domain. Other relevant claims of WO 01/9010188 teach as follows: Claims 2-3 teach use of homomultimerizing or heteromultimerizing receptors in the recombinant receptor; Claims 4-5 and 7 of WO 01/9010188 teach use of a bait that requires modification, such as phosphorylation, for binding of the prey molecule, and that the modification state is dependent on ligand binding; and claims 12, 14, and 16 teach use of a vector encoding the recombinant and eukaryotic cells comprising the vector.

WO 01/90188 does not teach a receptor wherein the receptor is inhibited by binding of a prey polypeptide to the bait polypeptide.

U.S. Patent No. 5,885,779 teaches a yeast two-hybrid system wherein the interaction of the bait and prey molecules causes inhibition of a transcriptional activator to which the bait is fused. This system can be used to screen for molecules that disrupt the bait-prey binding and lead to transcriptional activation. 5,885,770 further teaches (column 3, starting at line 60) advantages of using a system that relies on activation of a reporter to indicate disruption of bait-prey interaction. Such a system avoids pitfalls of a system relying on loss of a signal to indicate bait-prey disruption, wherein "failure to obtain expression may be caused by factors other than interference with the protein-protein interaction of interest. For example, compounds that interfere with transcription may score a false positive result. Similarly, compounds that generally inhibit cell growth

may score a false positive result by appearing to interfere with the expression of a reporter gene that would confer survival on a restrictive medium."

Nicholson teaches a protein, SOCS-3, which inhibits signaling of the cytoplasmic gp130 domain of a chimeric receptor by binding to the gp130 domain.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the cytoplasmic domain of a receptor such as gp130, which is inhibited by prey (SOCS-3) binding, for cytoplasmic domain of the receptor taught by WO 01/90188, which is activated by prey binding. The person of ordinary skill in the art would be motivated to do so because 5,885,779 teaches that screening for compounds that disrupt protein-protein interactions is best achieved with a system that reduces false positives, and Nicholson teaches a receptor based system where disruption of the protein-protein interaction leads to activation. One would expect success because WO 01/90188 teaches a receptor where prey binding activates the receptor, and teaches its use for screening prey-bait binding interactions, and in the absence of other evidence, one would expect a screen using an inhibitor would work just as well because such systems have been developed for transcriptional based two-hybrid systems.

It would further have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the recombinant receptor as taught in claims 2-5 and 7 of WO 01/90188, to produce a receptor as taught by these claims but wherein the receptor is inhibited by binding of a prey molecule. The person of ordinary skill in the art would be motivated to include an inhibitor for the same reasons as discussed above and because the further teachings of claims 2-5 and 7 are modifications of the receptor that allow for versatility in the type of receptors or bait used, and one would have expected success because, in the absence of other evidence, a receptor that is inhibited by prey binding would work just as well with these modifications as a receptor that is activated by prey binding.

It would further have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the vectors or eukaryotic host cell as taught in claims 12, 14, and 16 of WO 01/90188, to produce a vector that encodes a receptor that

is inhibited by prey binding, or a host cell comprising said vector. One would have been motivated to do so because of the motivation to produce a receptor that is inhibited by prey binding as described above, and because a vector and host cell is necessary to produce such a receptor, and one would have expected success because, in the absence of other evidence, such a vector or host cell would be expected to work just as well to produce a receptor inhibited by prey binding as a vector or host cell that produces a receptor that is activated by prey binding.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or is assigned is 571-273-2877.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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LORRAINE SPECTOR
PRIMARY EXAMINER